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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
WOODWARD, CHERIE MICHELLE	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 03/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/605,266	AKELLA ET AL.	
	Examiner	Art Unit	
	Cherie M. Woodward	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 December 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,18-23,26,28,29 and 33-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1-8, 26, 29, and 33-40* is/are allowed.

6)☒ Claim(s) *18-23 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04 November 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

1. Applicant's Response and Arguments filed 27 December 2005 is acknowledged. Claims 1-8, 18-23, 26, 28-29 and 33-40 are pending and under examination, as drawn to PDGF. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Arguments

Drawings

2. Applicants' request clarification as to the objection to the drawings, indicated by the Office Action Summary, filed 1 November 2005. The objection was a typographical error.

Claim Rejections Withdrawn

3. The rejection of claims 1-8, 28-29, and 33-40 under 35 USC 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps, has been fully considered and is persuasive. Applicants amendment of the phrase "depleted" to the word "excluded, which is defined in the specification at p. 4, line 32 to p. 5, line 1 is acknowledged. The rejection of claims 1-8, 28-29, and 33-40 under 35 USC 112, second paragraph for reciting the terms "depleted," "free", "substantially free," and "removed" has been withdrawn.

4. The rejection of claim 28 under 35 USC 112, second paragraph, as being indefinite for reciting multiple amino acid sequences with parenthesis around selected amino acids is moot in view of Applicants amendments to claim 28, deleting the parenthetical references.

5. The rejection of claim 8 under 35 USC 112, first paragraph, lack of enablement, is withdrawn pursuant to applicants' arguments, which were persuasive.

6. The rejection of claims 1-8, 18-23, 28-29, and 33-49 under 35 USC 112, first paragraph, scope of enablement is withdrawn in light of Applicants' arguments and the Cooper reference, which were persuasive.

7. The rejection of claims 1-8, 18-23, 26, 28-29, and 33-40 under 35 USC 112, second paragraph as being incomplete is withdrawn subsequent to Applicants' arguments, which were persuasive.

Claim Rejections Maintained

35 USC 112, second paragraph

8. The rejection of 28 as being improperly dependent on claim 1, under 35 USC 112, second paragraph, for failing to further limit the subject matter of a previous claim, is maintained for the reasons of record in the Office Action of 1 November 2005, and the reasons stated herein. Dependent claim 28 contains recited fragments of histone and ribosomal proteins that claim 1 recites as having been depleted. Thus, claim 28 improperly depends from claim 1.

Claim 1 has been amended to replace the term "depleted" with the term "excluded." Applicants argue that the term "excluded," as defined in the specification, recognizes that at least some, but not necessarily all histones and ribosomal proteins are excluded from the mixture. Applicant's arguments filed 27 December 2005 have been fully considered but they are not persuasive.

The term "excluded," as defined on page 4 of the specification (p. 4, lines 33-34 to p. 5, line 1), states that substantially all of the indicated component will be removed, to the extent the component can be removed with immunoaffinity chromatography or otherwise not included in the mixture. Where applicant acts as his or her own lexicographer to specifically define a term of a claim contrary to its ordinary meaning, the written description must clearly redefine the claim term and set forth the uncommon definition so as to put one reasonably skilled in the art on notice that the applicant intended to so redefine that claim term. *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1357, 52 USPQ2d 1029, 1033 (Fed. Cir. 1999). The term "excluded" in claim 1 is used by the claim to mean "that substantially all of the indicated component will be removed, to the extent the component can be removed with immunoaffinity chromatography or otherwise not included in the mixture", while the accepted meaning is "to keep out, to reject, to put out or expel" (see, for example, The American Heritage® Dictionary of the English Language, 2000). As such, the exclusion of histones and ribosomes from the bone protein mixture in claim 1 would preclude their presence in claim 28.

Claim Rejections - 35 USC § 103

9. The rejection of claims 18-23 under 35 U.S.C. 103(a) as being unpatentable over U.S Patent 6,177,406 (Wang *et al.*, 2001) in view of European application EP 0433225 A1 (Cerletti et al., 1991), and further in view of Stelincki *et al.* (Plastic and Reconstructive Surgery, 1998, vol. 101, pp. 12-19) (all previously cited in Office Action of 5 May 2003), is maintained for the reason of record in the Office Actions of 5 May 2003, 1 November 2005, and infra. Claims 18-23 recite a method for promoting healing of a skin wound.

Applicants argue that the references do not teach or suggest a bone-derived composition comprising all of BMP-2-3-4-5-6-7, TGFβ-1/2/3 and FGF-1, although the references teach BMP-3 and TGFβ-1/2/3. Applicants also argue that none of the references teach that native post-translational phosphorylation and glycosylation of the proteins they worked with is desireable or useful and that purification of the proteins should be undertaken with maintenance of post-translational modification. Applicant's arguments filed 27 December 2005 have been fully considered but they are not persuasive.

Wang *et al.*, specifically teach ground bovine bone in Example 1 (column 5-6). The pharmaceutical carrier of claim 18 is taught at column 4, lines 41-42. Use in wound healing, including burns, incisions, and ulcers, are taught at column 4, lines 28-31. Hydrogels are taught at column 4, lines 64-67 to column 5, lines 1-12. Extent of protein glycosylation is taught at column 7, line 58. Combinations including other growth factors, including EGF, PDGF, TGF, IGF, and FGF are taught at column 4, lines 52-55. Stelincki *et al.*, teach the use of BMP-2 to treat skin incisions in fetal lambs. Cerletti *et al.*, teach addition of copper to a TGF-β mixture on page 3, lines 52-54.

Applicants' arguments with respect to the desirability of maintaining post-translational modifications would be persuasive, but for the claim language of claim 20. Claim 20 recites the method of claim 18, wherein said proteins are at least partially phosphorylated and glycosylated. Even though Wang et al ('406 patent) teach that disruption of glycosylation sites in engineered BMP-3 is acceptable, Wang does not exclude glycosylated and phosphorylated bovine bone growth factors. Claim 20 reads on the necessity of only some of the growth factors being phosphorylated and glycosylated. It does not require preferential preservation of phosphorylation and glycosylation nor does it preclude some of the proteins from being be denatured and renatured. The phrase "at least partially" in claim 20 recites a very low standard for and suggests no degree of phosphorylation and glycosylation that should be maintained. Instead it merely

suggests that some amount of phosphorylation and glycosylation be maintained in at least some proteins within the protein mixture.

It would have been obvious to one of ordinary skill in the art to combine the teachings of Wang *et al.*, Stelincki *et al.*, and Cerletti *et al.*, to combine three or more growth factors (including, but not limited to BMP-4, BMP-5, BMP-6, BMP-7, and FGF-1) for wound healing, particularly when the multiple factors are related growth factors that are all present in the ground bovine bone mixtures, as taught by Wang *et al.* One of ordinary skill would be motivated to combine multiple BMPs, TGF-β-1/2/3, and FGFs for the reasons that all of the growth factors are already in the ground bovine bone mixture and they are all known to be useful for the same or a similar purpose. The skilled artisan would have reasonably expected success because all of the claimed growth factors, which are known in the art to promote wound healing, were already naturally present in the ground bovine bone mixture taught by Wang *et al.*

New Claim Objection/Rejection – Necessitated by Amendment

10. Claim 28 is objected to because of the following informalities: SEQ ID NO: 24 is identical to SEQ ID NO: 32. Although the SEQ ID NOs were not originally submitted in the original filing, the sequence listing is supported by Figures 15A and 15B, including the disclosed amino acid variances listed. However, it is improper for the same sequence to be identified by two different SEQ ID NOs. Appropriate correction is required.

Conclusion

11. Claims 1-8, 26, 29, and 33-40 are allowable.

Applicant's amendment necessitated the new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cherie M. Woodward whose telephone number is (571) 272-3329. The examiner can normally be reached on Monday - Thursday 9:00am-7:30pm (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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